PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Hyun-Soo KIM, et al.

Docket No: Q94674

Appln. No.: 10/595,620

Group Art Unit: 1633

Confirmation No.: 3640

Examiner: Fereydoun Ghotb SAJJADI

Filed: May 1, 2006

For: METHOD FOR DIFFERENTIATING MESENCHYMAL STEM CELL INTO NEURAL CELL AND PHARMACEUTICAL COMPOSITION CONTAINING THE NEURAL CELL FOR NEURODEGENERATIVE DISEASE

SUBMISSION OF EXECUTED DECLARATIONS UNDER 37 C.F.R. §1.132

MAIL STOP PCT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Sir:

Submitted herewith is a copy of an executed Declaration Under 37 C.F.R. §1.132 signed by Mr. Hyun-Soo Kim.

Acknowledgement of these documents is requested.

Respectfully submitted,

/Sunhee Lee/

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WASHINGTON OFFICE
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CUSTOMER NUMBER

Date: July 6, 2009

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DECLARATION UNDER 37 C.F.R. § 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Hyun-Soo KIM, hereby declare and state:

THAT I am a citizen of South Korea;

THAT I have received a medical degree from Yonsei University, Wonjoo School of Medicine, South Korea and a Ph.D. degree in Hematology Medical Oncology from AJoo University, School of Medicine, South Korea;

THAT I was employed by FCB Pharmicell Co., Ltd. as a board member from May, 2002 till June, 2004 and also have been employed as a Chief of FCB Pharmicell Cell Treatment Center from October, 2002 till present, with responsibility for sub-managing;

THAT I have been a professor in Hematology Medical Oncology at AJoo University, School of Medicine since November, 2003 and at Yonsei University, Wonjoo School of Medicine since March 2005.

THAT I am one of the inventors of the above mentioned application;

THAT I have read the Office Action dated April 29, 2008, and January 6, 2009, and understand the basis of the rejections set forth therein and the references cited by the Examiner, particularly Fercht et al. and Kokuzawa et al.; and

THAT Fercht et al. and Kokuzawa et al. does not disclose all elements defined in the claims of the instant application or unexpected properties obtained from the invention.

The specification of the instant application shows that the presently claimed method of differentiating mesenchymal stem cell (MSC) with a prior confluent culture shows unexpectedly superior results.

Table 3 of the specification, as reproduced below, demonstrates that, after being cultured for two weeks with EGF and HGF, while cells without a prior confluent culture results in only 30 % differentiation, cells with a prior confluent culture results in 90 % differentiation after 2 weeks. Thus, this results proves that differentiating MSCs with the prior confluent culture increased the differentiation rate of MSCs by three times at the two-week point.

Moreover, even if cells without a prior confluent culture are continued to be cultured up to four weeks, they result in only 80 % differentiation, which still is lower than the differentiation result of those with a prior confluent culture after two weeks.

Accordingly, Applicants' method of differentiating MSC with a prior confluent culture results in unexpectedly superior differentiating rate of MSCs.

TABLE 3

	Time (week)	NSE	NeuN	GFAP	Map 2	Negative cells
Only EGF	4	0.9%	0.8%	1.2%	—	89%
EGF + HGF	2	10%	25%	4%	—	70%
EGF + HGF	4	56%	75%	24%	—	20%
EGF + HGF After confluent culture for 24 hours.	2	62%	88%	31%	11%	10%

Moreover, above-mentioned results of increased differentiating rate of MSCs are significant for an effective MSC treatment of a patient. It is because previous *in vivo* experimental results show that a patient must be treated with MSC at an early stage of a defect for a more effective functional recovery.

For example, Iihoshi *et al.* (A therapeutic window for intravenous administration of autologous bone marrow after cerebral ischemia in adult rats. Brain Research 1007: 1-9, 2004; attached hereinwith) used an *in vivo* rat model with middle cerebral artery occlusion (MCAO) and showed that an earlier injection of MSCs results in a smaller lesion volume, higher MSC proliferation and more functionality of differentiated cells, compared to a later injection of MSCs.

Omori *et al.* (Optimization of a therapeutic protocol for intravenous injection of human mesenchymal stem cells after cerebral ischemia in adult rats. Brain Research 1236: 30-38, 2008; attached hereinwith) injected human MSCs into an *in vivo* MCAO animal model and also

showed that it is more effective to inject MSCs at an early state, such as acute phase or subacute phase of cerebral infarction.

Applicants' method of differentiating MSC with a prior confluent culture results in faster differentiation of MSCs, which can be applied to a patient sooner and at an earlier stage of differentiation than those differentiated without a prior confluent culture, such as those of Furcht et al. This is clinically important in that it makes a MSC treatment more effective. Accordingly, Applicants' method of differentiating MSC with a prior confluent culture results in unexpectedly superior MSC treatment of a patient.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 03/July/2009

Hyun-Soo KIM